The Examiner notifies Applicants that the drawings are objected to by the Draftsperson as informal. Applicants have filed with informal drawings, which are acceptable for examination. Formal drawings will be provided in a timely manner.

Claims 1-12 remain pending in the application and under consideration by the Examiner. Claim 1 has been amended to recite "wherein endoreduplication in the cell is modulated". Support for the amendment can be found throughout the specification, including the Examples and in the preamble of the original claim. The subject matter of claims 2 and 8 have been incorporated into claims1 and 7 respectively. Claim 7 has been amended to include steps of growing the transformed plant cell to produce a regenerated plant having cells exhibiting increased endoreduplication. Support for the amendment is found throughout the application and in particular in Example 2, pages 22-23. No new matter has been added by amendment.

Claims 7-12 were rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains... to make and/or use the invention.

The Examiner states "[t]he specification does not teach whether an increase in endoreduplication brought about by the introduction of an isolated viral replicase polynucleotide into a plant cell will also bring about an increase in crop yield...".

Example 2 in the specification and Exhibits 1 and 2 of the 1.132 Declaration provide results indicating that in maize and in soybean plants transformed with a RepA expression cassette, transgenic plants can be regenerated in which the ploidy level has increased from diploid to tetraploid, i.e. endoreduplication has occurred. In both maize and soybean, the regenerated tetraploid plants were substantially larger than diploid plants. In soybean, in which successful crosses were completed with these RepA+ tetraploid plants, the resultant T1 progeny inherited this "giant" phenotype as described on page 2 of the Declaration and as shown in Exhibit 2 of the Declaration.

The Examiner cites Larkins et al. (Journal of Experimental Botany, February 2001, Vol. 52, No. 355, pages 183-192), and stated that "Larkins et al. teach that the physiological significance of endoreduplication is poorly understood." The Examiner further states that it is not known whether increased endoreduplication may be correlated with increased crop yield.

A 1.132 Declaration is submitted providing evidence in support of the present claims relating to increased crop yield.

Exhibit 1 of the Declaration demonstrates a doubling in overall cellular DNA content (i.e. from diploid to tetraploid) in cells transformed with RepA compared to cells that have not been transformed.

Exhibit 2 demonstrates that RepA+ soybeans express a "giant" phenotype as a result of increased endoreduplication. From this observation and the literature cited in the Declaration the Applicant submits that increased crop yield is expected to result from the transformed plants.

The Examiner further asserts that it would require undue experimentation to increasing the yield of crops through increased endoreduplication using all methods known to one of ordinary skill in the art, in order to practice Applicant's invention as broadly claimed.

However, when determining the quantity of experimentation necessary, the focus is not on the amount of experimentation necessary to practice the entire genus, but the amount of experimentation required to practice any particular member. This concept is the central holding of *In re Wands* where the claims read on the use of any IgM antibody that possessed a particular binding affinity. This is similar to the present case where the claims read on increasing the yield of any crop through increased endoreduplication greater than the wild type. The *Wands* court recognized that it would require an infinite amount of experimentation to obtain every single possible IgM antibody that could be generated with the specified affinity. Accordingly, the court focused on the amount of experimentation necessary to practice any particular IgM antibody with the recited binding affinity and not the

amount of experimentation required to practice the entire genus. This focus is further supported by the multitude of chemical patents that have issued with generic claims reading on tens to hundreds of thousands of individual members.

The question then becomes how much experimentation is required to create the claimed methods of the invention for increasing crop yield through increased endoreduplication. Applicants submit that no more than routine experimentation is required. They may be accomplished by the examples and methods within the present application and within the technical, scientific, skill in the art.

Applicants assert the present invention is disclosed in a way that one skilled in the art will be able to practice it without an undue amount of experimentation. *In re Borkowski*, 422 F.2d 904, 908, 164 USPQ 642, 645 (CCPA 1970). Applicants submit that they have fully enabled the present invention as claimed by teaching both how to make and how to use the invention. Applicants have specifically taught methods of increasing endoreduplication in nuclei isolated from transgenic plants as compared to nuclei isolated from wild type plants (pages 21-24 Examples 1 and 2). Therefore, one of ordinary skill could use Applicants' teachings to provide an increase in the yield of a crop through increased endoreduplication as taught by Applicant.

The USPTO carries the initial burden to establish a reasonable basis for questioning the enablement provided for the claimed invention. As stated in *In re Wright*, 99, F.2d 1557, 27 USPQ2d 1510 (Fed. Cir. 1993); MPEP § 2164.04, the enablement requirement is satisfied if the specification describes any method for making and using the claimed invention that bears a "reasonable correlation" to the entire scope of the claims. Applicants submit that this has been accomplished in the present application.

Claim 1 was rejected by the Examiner under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The Examiner has rejected Claim 1 because the term "or" is unclear whether the promoter is driving expression in the target cell, or driving expression in an isolated viral replicase. Applicants have rewritten claim 1 to clarify what the promoter is driving.

The Examiner has rejected Claims 1-2, 4-8, and 10-11 under 35 U.S.C. § 102(e) as being anticipated by Gronenborn (US 6,133,505 October 17, 2000). Claims 2 and 8 have been canceled without prejudice.

The Examiner states, "[t]he claims are drawn to a method of introducing into a plant target cell an isolated plant geminivirus viral replicase polynucleotide operably linked to a promoter, wherein the plant is the dicot tomato". The Examiner further suggests that Gronenborn teaches the same method.

Gronenborn disclose mutating RepA as a viral resistance mechanism. The Gronenborn invention relates to transgenic plants that are resistant or tolerant to DNA viruses that are pathogenic in plants (column 1, lines 8 through 18).

In contrast, the present invention provides a method for modulating endoreduplication through transgene manipulation. The present invention provides novel methods of using viral replicase polypeptides and polynucleotides. Included are methods for increasing crop yield.

Anticipation requires that each element and limitation of the claimed invention be known or used by others prior to the invention by the patentee. *Oney v. Ratliff*, 182 F.3d 893, 895, 51 USPQ.2d 1697 (Fed. Cir. 1999). Additionally, the MPEP 2131, page 2100-54, states, "[t]o anticipate a claim, the reference must teach every element of the claim. A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." Thus, Gronenborn does not anticipate the claims, and the rejection under 35 U.S.C. § 102 should be withdrawn.

The Examiner has rejected Claims 1-12 under 35 U.S.C. § 103(a) as being unpatentable over Gronenborn (US 6,133,505 October 17, 2000) in view of Grafi et

al. (Proc. Natl. Acad. Sci. USA, August 1996, Vol. 93, pages 8962-8967, Applicant's ISD).

The Examiner states "it would have been *prima facie* obvious to one with ordinary skill in the art at the time the invention was made to introduce a viral replicase polynucleotide into a cell as taught by Gronenborn, for the purpose of increasing endoreduplication, given the teachings of Grafi et al. that the viral LxCxE motif proteins encoded by such polynucleotides could inactivate retinoblastoma proteins and cause a transition from the G1 to the S phase of the cell cycle, thus increasing endoreduplication".

As discussed in the present 1.132 Declaration, it is well documented that proliferation of mammalian cells can be stimulated by expression of certain proteins, but it should be emphasized that in such examples this is a stimulation of the mitotic cell cycle and not endoreduplication.

As discussed above, the present claims require modulating or increasing endoreduplication to increase crop yield resulting from a method of introducing into a plant cell an isolated plant viral replicase polynucleotide. As indicated by the Examiner the teaching of Gronenborn show no recognition of increasing crop yield by a method of increased endoreduplication. *Id.* "[I]t is the invention as a whole that must be considered in obviousness determinations. The invention as a whole embraces the structure, its properties, and the problems it solves." *In re Wright*, 848 F.2d 1216, 6 USPQ2d 1959 (Fed. Cir. 1988).

In addition, there is no suggestion or motivation from the items cited by the Examiner as to why one of ordinary skill in the art would have been led to produce the claimed invention. In the absence of such reason or suggestion, a prima facie case of obviousness is not shown. There must also be some reasonable expectation of success relating to the prior art that must make any proposed modification or changes in the prior art obvious to do rather than obvious to try. As the Federal Circuit stated in the case of *In re O'Farrell:*

"...what was obvious-to-try" was to explore a new technology or general approach that seemed to be a promising field of experimentation, where the prior art gave only general guidance as to the particular form of the claimed invention of how to achieve it." 853 F. 2d at 903, 7 USPQ 2d at 1681

Thus, obvious-to-try is not a proper basis for rejecting the claims under 35 U.S.C. §103 because there is no suggestion or expressed expectation of success in the prior art that would have led one to perform the experimentation in the first place.

In view of these remarks, Applicants respectfully submit that the claimed invention is not disclosed or suggested by the items cited by the Examiner.

Applicant respectfully submits that in light of the foregoing amendments and remarks, allowance of the remaining claims is respectfully requested. If prosecution toward allowance could be furthered by a telephone call to the undersigned attorney for Applicant (515-334-4467), one is earnestly requested.

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Specification:

On page 3, line 6 the following paragraph has been inserted:

BRIEF DESCRIPTION OF THE DRAWINGS

Figure I represents flow cytometric analysis of nuclei from plant tissue that has not been transformed with RepA and of nuclei from plant tissue transformed with RepA.

In the Claims:

Claims 2 and 8 have been canceled without prejudice or disclaimer.

Claims 1, 3, 7 and 9 have been amended as follows:

1. (Once Amended) A method for modulating endoreduplication comprising introducing into a target cell an isolated [viral] plant geminivirus replicase polynucleotide or an isolated plant geminivirus replicase polypeptide, wherein the polynucleotide is operably linked to a promoter driving expression in the target cell [or an isolated viral replicase polypeptide] and wherein endoreduplication in the cell is modulated.

3. (Once Amended) The method of claim [2] 1 wherein the polynucleotide is wheat dwarf virus [Replicase] RepA.

7. (Once Amended) A method for increasing crop yield through increased endoreduplication comprising introducing into a plant cell an isolated [viral] plant geminivirus replicase polynucleotide operably linked to a promoter driving expression in the plant cell to produce a transformed plant cell, and

growing the transformed plant cell under conditions sufficient to produce a regenerated plant having cells exhibiting increased endoreduplication.

9. (Once Amended) The method of claim [8] 7 wherein the polynucleotide is wheat dwarf virus [Replicase] RepA.